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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/779,461	02/09/2001	Peet Kask	P64765US1	6710

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EXAMINER	
LEE, SHUN K	

ART UNIT	PAPER NUMBER
2878	

DATE MAILED: 05/08/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Offic Action Summary	Application No. 09/779,461	Applicant(s) KASK, PEET	
	Examiner Shun Lee	Art Unit 2878	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 February 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-17* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *09 February 2001* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *4* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Information Disclosure Statement

1. The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609 A(1) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered.

Drawings

2. The drawings are objected to because:

(a) in Figs. 1 and 3, "Figur" should be --FIG.-- (it should be noted that view numbers must be preceded by the abbreviation "FIG.", see 37 CFR 1.84(u)(1)); and

(b) Fig. 5 is not legible.

A proposed drawing correction or corrected drawings are required in reply to the Office action to avoid abandonment of the application. The objection to the drawings will not be held in abeyance.

3. The drawings are objected to as failing to comply with 37 CFR 1.84(p)(5) because they include the following reference sign(s) not mentioned in the description: 46 and 48 (Fig. 7). A proposed drawing correction, corrected drawings, or amendment to the specification to add the reference sign(s) in the description, are required in reply to the Office action to avoid abandonment of the application. The objection to the drawings will not be held in abeyance.

Specification

4. Applicant is reminded of the proper language and format for an abstract of the disclosure.

The abstract should be in narrative form and generally limited to a single paragraph on a separate sheet within the range of 50 to 150 words. It is important that the abstract not exceed 150 words in length since the space provided for the abstract on the computer tape used by the printer is limited. The form and legal phraseology often used in patent claims, such as "means" and "said," should be avoided. The abstract should describe the disclosure sufficiently to assist readers in deciding whether there is a need for consulting the full patent text for details.

The language should be clear and concise and should not repeat information given in the title. It should avoid using phrases which can be implied, such as, "The disclosure concerns," "The disclosure defined by this invention," "The disclosure describes," etc.

5. The abstract of the disclosure is objected to because it is not a single paragraph in narrative form and because of the language. Correction is required. See MPEP § 608.01(b).

6. The disclosure is objected to because of the following informalities:

(a) brief description of the drawings is missing; and

(b) section headings (*e.g.*, Background of the Invention, Brief Summary of the Invention, Brief Description of the Several Views of the Drawings, and Detailed Description of the Invention) should be provided.

Appropriate correction is required.

7. The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

Claim Objections

8. Claims 14 and 17 are objected to because of the following informalities:

(a) on line 2 in claim 14, "wavelenghts" should probably be --wavelengths--; and

(b) on line 4 in claim 17, "focussing" should probably be --focusing--.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

9. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. Claims 8 and 17 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Regarding claims 8 and 17, the phrase "preferably" renders the claims indefinite because it is unclear whether the limitation(s) following the phrase are part of the claimed invention.

Claim Rejections - 35 USC § 102

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

12. Claims 1-6 and 12-16 are rejected under 35 U.S.C. 102(b) as being anticipated by Kask (EP 0 884 583 A1).

In regard to claim **1**, Kask discloses (pg. 3, lines 33-39) a method for characterizing samples having fluorescent particles, comprising the steps of:

(a) monitoring intensity fluctuations of fluorescence emitted by the particles in at least one measurement volume by detecting sequences of photon counts by at least one photon detector (pg. 4, lines 8-16),

(b) determining from the sequences of photon counts intermediate statistical data comprising at least two probability functions, $\mathbf{P}_1(n_1)$, $\mathbf{P}_2(n_2)$, ..., of the number of photon counts, n_1, n_2, ..., detected in different sets of counting time intervals (pg. 3, line 40 to pg. 4, line 3),

(c) determining from said intermediate statistical data a distribution of particles (i.e., concentration of units; pg. 3, lines 33-39) as a function of at least two arguments, wherein one argument is a specific brightness of the particles, or a measure thereof, and another argument is a diffusion coefficient of the particles, or a measure thereof (pg. 4, lines 17-34).

In regard to claim **2** which is dependent on claim 1, Kask also discloses (pg. 3, lines 40-58) that each set of counting time intervals consists of intervals of equal width while different probability functions $\mathbf{P}_{T1}(n_1)$, $\mathbf{P}_{T2}(n_2)$, ..., correspond to counting time intervals of different width T_1, T_2, ...

In regard to claim **3** which is dependent on claim 1, Kask also discloses (pg. 3, lines 40-58) that in each set of counting time intervals these intervals are consecutive in time.

In regard to claim **4** which is dependent on claim 1, Kask also discloses (pg. 3, lines 40-58) that counting time intervals are consecutive in a preferred embodiment. Thus, it is inherent that there exist embodiments with non-consecutive (*i.e.*, overlap) counting time intervals.

In regard to claim **5** which is dependent on claim 1, Kask also discloses (pg. 5, lines 38-49) that said distribution function of particles is determined by fitting the experimentally determined probability functions $\mathbf{P}_1(n_1)$, $\mathbf{P}_2(n_2)$, ... by corresponding theoretical probability functions $P_1(n_1)$, $P_2(n_2)$, ...

In regard to claim **6** which is dependent on claim 1, Kask also discloses (pg. 5, lines 38-49) that said intermediate statistical data are processed applying inverse transformation with regularization and/or constraints.

In regard to claim **12** which is dependent on claim 1, Kask also discloses (table 1 on pg. 7) that concentrations of particles are selected to be approximately one or less molecules per measurement volume.

In regard to claim **13** which is dependent on claim 1, Kask also discloses (pg. 4, lines 11-13) that said photon detector is either an avalanche photodiode or a photomultiplier.

In regard to claim **14** which is dependent on claim 1, Kask also discloses (pg. 4, lines 8-16) that at least two photon detectors are used monitoring fluorescence of different wavelengths or polarization.

In regard to claim **15** which is dependent on claim 1, Kask also discloses (pg. 4, lines 22-28) that said fluorescent particles are characterized applying an homogeneous fluorescence assay (*i.e.*, fluorescence assay of non-separated mixtures).

In regard to claim **16** which is dependent on claim 1, Kask also discloses (pg. 4, line 42 to pg. 5, line 30) a method for use in diagnostics, high throughput drug screening, optimization of properties of molecules and identification of specific cell populations.

Claim Rejections - 35 USC § 103

13. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

14. Claims 7-11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kask (EP 0 884 583 A1) in view of Palo (US 6,376,843).

In regard to claims **7-11** which are dependent on claim 1, Kask is applied as in claim 5. The method of Kask lacks that the theoretical distributions $P_1(n_1)$, $P_2(n_2)$, ... are calculated through their generating functions $G_{p(n)}(\xi) = \Sigma_n \xi^n \cdot P(n)$, where the generating function is calculated using the expression $G(\xi) = \exp[\int dq c(q) \int d^3r (e^{(\xi-1)qTB(r)} - 1)]$, where c(q) is the density of particles with specific brightness q, T is the length of the counting time interval, B(r) is the spatial brightness profile as a function of coordinates and that the relationship between the spatial brightness B and volume elements dV is expressed through a variable $x = \ln(B_o/B)$ by a relationship $dV/dx = A_o (1 + a_1 x + a_2 x^2) x^{a_3}$, where B_o

is maximum brightness and A_o, a_1, a_2 and a_3 are empirical parameters of the spatial brightness function. Palo teaches (Eq. 8 in column 4; column 5, lines 3-11 and 38-50) that the theoretical distributions $P_1(n_1)$, $P_2(n_2)$, ... are calculated through their generating functions $G_{p(n)}(\xi) = \Sigma_n \xi^n \cdot P(n)$, where the generating function is calculated using the expression $G(\xi) = \exp[\int dq c(q) \int d^3r (e^{(\xi-1)qTB(r)} - 1)]$, where c(q) is the density of particles with specific brightness q, T is the length of the counting time interval, B(r) is the spatial brightness profile as a function of coordinates and that the relationship between the spatial brightness B and volume elements dV is expressed through a variable $x = \ln(B_o/B)$ by a relationship $dV/dx = A_o (1 + a_1x + a_2x^2)x^{a_3}$, where B_o is maximum brightness and A_o, a_1, a_2 and a_3 are empirical parameters of the spatial brightness function in order to minimize the time needed for analyzing fluorescence intensity fluctuations. Therefore it would have been obvious to one having ordinary skill in the art to calculate the theoretical distributions $P_1(n_1)$, $P_2(n_2)$, ... in the method of Kask using the generating functions of Palo, in order to minimize the time needed for analyzing fluorescence intensity fluctuations as taught by Palo.

15. Claim 17 is rejected under 35 U.S.C. 103(a) as being unpatentable over Kask (EP 0 884 583 A1) in view of Dorsel (US 6,222,664).

In regard to claim **17** which is dependent on claim 1, Kask also discloses (pg. 6, lines 6-10) that the method includes a confocal apparatus comprising: an excitation radiation (*i.e.*, incident laser beam) which is inherently provided by a laser (*i.e.*, radiation source), an objective for focusing the excitation radiation into a measurement volume, and a detector (pg. 4, lines 8-16) for detecting emission radiation that stems from the

measurement volume. The method of Kask lacks an opaque means positioned in the pathway of the emission radiation or excitation radiation for erasing the central part of the emission radiation or excitation radiation. Dorsel teaches (column 1, lines 9-25) that confocal systems are well known in the art and to provide an opaque means positioned in the pathway of the emission radiation or excitation radiation for erasing the central part of the emission radiation or excitation radiation (column 4, lines 18-22) in order to suppress light originating outside the intended detection plane (column 1, lines 47-50). Therefore it would have been obvious to one having ordinary skill in the art to provide an opaque means positioned in the emission or excitation radiation pathway in the method of Kask, in order to suppress light originating outside the intended detection plane as taught by Dorsel.

Double Patenting

16. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

17. Claims 1-6 and 12-17 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-19 of U.S.

Patent No. 6,208,815. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant application recites the limitation "intermediate statistical data comprising at least two probability functions" and US 6,208, 815 recites the limitation of "at least one set of statistical data or at least one combination of several sets of statistical data" (for the determination of particle properties in a confocal system; see instant claim 17 and US 6,208, 815 claim 11). An intermediate statistical data comprising at least two probability functions is at least one combination of several sets of statistical data and thus the claims are not patentably distinct from each other.

18. Claims 1-6 and 12-17 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 24-112 of copending Application No. 09/445,428. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant application recites the limitation "intermediate statistical data comprising at least two probability functions" and copending Application No. 09/445,428 recites the limitation of "intermediate statistical data comprising a probablity function of at least two arguments" (for the determination of particle properties in a confocal system; see instant claim 17 and copending Application No. 09/445,428 claims 46, 67, 88, and 109). An intermediate statistical data comprising at least two probability functions is a probablity function of at least two arguments and thus the claims are not patentably distinct from each other.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

19. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. US Patent 6,208,815 (Seidel *et al.*).

20. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shun Lee whose telephone number is (703) 308-4860. The examiner can normally be reached on Tuesday-Thursday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Seungsook Ham can be reached on (703) 308-4090. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 872-9318 for regular communications and (703) 872-9319 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0956.

CONSTANTINE HANNAHER
PRIMARY EXAMINER
GROUP ART UNIT 2878

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May 1, 2002